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International Preliminary
Examining Authority

Fax.: 0049 89 2399 4465

Rio, September 13, 2001

Ref.: **PCT** - International Application PCT/BR00/00077
filed on 14.07.2000
INDUSTRIA E COMERCIO DE COSMÉTICOS NATURA
Our ref.: PE-3933 (MCB)

Dear Sirs,

In response to the first written opinion issued on the above case, the applicant firstly presents new pages of the specification, a new set of claims and a new abstract in order to correct the irregularities mentioned by the examiner. The amendments and modifications are as follows:

a) the quantitative values represented by decimal fractions have been corrected throughout the specification and claims;

b) the definition of Dequest 2010 ® has been corrected to "1- hidroxyethylidene (1,1 diphosphonic) acid (new page 7, lines 8-9, 12-13 and 18, Example 1 and claims 7, 15 and 16);

c) the term "biphasic" has been deleted throughout the specification in order to avoid any unclearness. As is clear from the description, the composition of the invention comprises two distinct phases, which phases are precisely defined both qualitatively and quantitatively. Therefore, the term biphasic was considered indeed unnecessary.

d) the dependency relationship of claims 3 was reformulated. It should be noticed that claims 2 and 3 define two different embodiments of the invention, that is, the two different ranges within which acid ascorbic (LAA) presents the antioxidant action desired in the present composition. Therefore, according to the present invention, when LAA is used as the antioxidant, it may be used either in a range from 1% to

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30%, by weight (claim 2) or from 0.0001% to 0.001% (claim 3). Both alternatives are described in the specification.

e) the term "reaction oxidation reverting compound" was redrafted as "reducing agent". As far as the expression "deoxygenating compound" is concerned, it is observed that the definition thereof is set forth on page 6, lines 18-20, of the specification and refers to "any compound or mixture of compounds able to diminish the oxygen solubility in a medium containing water and the antioxidant to be stabilized". This definition meets with the one specifically mentioned in the written opinion and, consequently, no modification was carried out thereon.

f) Claim 8 has been restricted with the specific proportion between the two phases, wherein the second phase is now precisely defined.

Applicant respectfully submits that the above amendments are fully supported on the application as originally filed and do not represent addition of new matter.

According to the Written Opinion, the present claims are objected as not being novel when compared with documents D1. D2 and D3 mentioned in the International Search Report. Applicant, however, respectfully observe that none of the mentioned prior art references discloses a composition as claimed in the present application.

Firstly it should be noticed that the present claim 1 refers to a composition comprising two distinct phases, one aqueous phase comprising an antioxidant and a second phase which comprises a moisturizer compound and an immunomodulator and the proportion of said first phase to the second phase being from 6:1 to 14:1. In the same way present claim 8 defines a composition comprising two phases with a specific proportion between them. Thus, the present application does not aim to claim any composition comprising those compounds. Such a composition would indeed be already known from the prior art. The new feature of the claimed composition is the fact that its ingredients are present in specific and distinct phases and that said two phases are present in a particular proportion.

None of the mentioned prior art references discloses compositions with the components divided in such different phases nor define a proportion between those phases as defined in the present application. It is, therefore, concluded that the present claims meet the criteria of novelty over the mentioned prior art.

Apart from the above comments directed to the novel aspects of the present application, it should also be pointed out that the claimed composition provides new

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and unexpected technical effects over the prior art.

The composition as described in D1 must comprise a considerable number of chemical compounds to achieve the desired results. The composition of the present invention, on the other hand, overcome the prior art technical problems and makes it possible to reduce the number of necessary ingredients while achieve improved stability and cosmetic results (please see comments on page 2, lines 14 to 16, of the present specification).

D2 discloses compositions containing some components analogous to those used in the present composition. But again it is stressed that the composition claimed in the application is restricted to a specific division of the components within two distinct phases and those phases are present in a particular proportion. Moreover, D2 (page 31, line 25 to 29) mentions the drawbacks derived from the instability of Vitamin C which leads to the conclusion that those inventors did not develop a stabilized composition.

In fact, the compositions disclosed in D1 and D2 use derivatives of Vitamin C, namely a chemically modified derivative which is already stabilized (magnesium ascorbyl phosphate) and there is no mention that Vitamin C in its molecular form could be used without facing problems with its instability. Thus, neither D1 nor D2 mention nor foresee a composition in which Vitamin C (LAA) could be used in a stabilized form, as in the present invention.

D3 refers to stable emulsions containing ascorbic acid. However, such compositions necessarily comprise an organoclay material. Therefore, the technical effect obtained in accordance with those inventors is to produce a composition where the ascorbic acid is present in a liquid medium provided that a organoclay (e.g, bentonite) is added thereto. That document shows that bentonite surface is treated with ammonium chloride compound (claim 9). Such a modified composition has a positive charge in the presence of water while ascorbic acid would have a negative charge. It would provide an ionic or electrokinetic interaction between those two components.

The teachings of that prior art document does not anticipate the composition as present claimed which does not comprise a clay . In addition, D3 would never lead someone skilled in the art to develop the present composition with its two distinct phases and with a particular proportion between them without any addition of clay or similar material.

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In view of the clarifications presented above, the applicant respectfully submits that the invention as now claimed is novel and inventive over the prior art represented by D1, D2 and D3 .

Very truly yours

Maria Carmen S. Brito
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PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

WRITTEN OPINION

(PCT Rule 66) 01

Date of mailing *(day/month/year)*	31.07.2001
Applicant's or agent's file reference: PE-3933	**REPLY DUE** **within 1 month(s) and 15 days** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/BR00/00077	14/07/2000	16/07/1999

International Patent Classification (IPC) or both national classification and IPC

A61K7/00

Applicant

INDUSTRIA E COMERCIO DE COSMETICOS NATURA LTDA.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 16/11/2001.

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Authorized officer / Examiner
Pregetter, M

Formalities officer (incl. extension of time limits)
Longo, E
Telephone No. +49 89 2399 8141

I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

   Description, pages:

   1-12 as originally filed

   Claims, No.:

   1-21 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-21
Inventive step (IS)	Claims	
Industrial applicability (IA)	Claims	

2. Citations and explanations
   see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: US-A-5 804 168 (MURAD HOWARD) 8 September 1998 (1998-09-08)
   D2: WO 99 33439 A (ROBERTS RICHARD L ;GREENE JAMES A (US); SHAKLEE CORP (US); SIDDIQU) 8 July 1999 (1999-07-08)
   D3: US-A-5 902 591 (HERSTEIN MORRIS) 11 May 1999 (1999-05-11)

2. The subject-matter of present claim 1 is not novel according to Article 33(2) PCT.
   Document D1 discloses aqueous emulsions comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (propylene glycol and/or butylene glycol), a metallic ions sequestering compound (EDTA), and, in the dispersed phase, immunomodulators (retinyl and/or ascorbyl palmitates) and moisturizers/emollients (col.13, l.25-64 and col.15, l.55-col.16, l.24).
   D2 describes an oil-in-water formulation comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (the most common humectants are glycols), a metallic ions sequestering agent, and, in the dispersed phase, immunomodulator (beta glucan) and moisturizers/emollients. Proanthocyanidins in the form of grape seed extract are also present (e.g. example 6).

3. The subject-matter of present claim 8 is not novel according to Article 33(2) PCT.
   D2 describes an oil-in-water formulation comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (the most common humectants are glycols), a metallic ions sequestering agent, a reducing agent (superoxide dismutase), and, in the dispersed phase, immunomodulator (beta glucan) and moisturizers/emollients (e.g. example 6).
   D3 discloses a mixture of 5% powdered ascorbic acid with 95% of an emulsion resulting in dissolving the ascorbic acid in the aqueous phase of said emulsion. The resulting aqueous phase comprises the ascorbic acid (antioxidant), a

deoxygenating agent (butylene glycol), a metallic ions sequestering compound (EDTA) and a reducing agent (superoxide dismutase).

4. With regard to the dependent claims, it is noted that a positive opinion can only be given, if dependent claims refer to independent claims that meet the requirements of the PCT.
Furthermore, the following has to be noted:
The use of a substance in certain percentages can only be considered to involve an inventive step, if it can be clearly shown that said percentages are unusual in the art and lead to a surprising effect.
The use of a specific immunomodulator, reducing agent, sequestering agent, ... can only be considered to involve an inventive step, if such a use is unusual in the art and leads to a surprising effect. However, the combination of specific compounds in specific percentages is very often not suggested by the prior art.

5. In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT).
In case of non-compliance, said amendments cannot be taken into account when establishing the international preliminary examination report.

Re Item VII
Certain defects in the international application

1. According to Rule 10(f) PCT the beginning of a decimal fraction has to be marked by a period.

2. The description is not in conformity with claims 7-21 as required by Rule 5.1(a)(iii) PCT.

Re Item VIII
Certain observations on the international application

1. The term "biphasic" used throughout the claims is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of the claims unclear (Article 6 PCT).
   The term "biphasic" can relate to either solid/liquid or liquid/gaseous compositions (or others) or to hydrophilic/hydrophobic compositions such as dispersions (or very often emulsions). Furthermore, according to the statement on p.3, l.29-p.4, l.4, the term "biphasic" can also refer to two phases which are separately packaged, although the term "phases" does not seem to be a very fitting term for two solutions which are separately packaged.
   Present claim 8 does not even define any second "phase".
   For the purpose of preliminary examination all possibilities have to be taken into consideration.

2. The term "preferably" does not limit the scope of a claim in any way.

3. Present claim 3 cannot depend on claim 2, because the range of 0.0001 to 0.001% by weight is not included in the range given in claim 2 (Article 6 PCT).

4. The use of parenthesis and abbreviations in claims leads to a lack of clarity (Article 6 PCT).

5. The term "Dequest" employed in claim 7 and appearing to be a registered trade mark has no precise meaning as it is not internationally accepted as a standard descriptive term, thereby rendering the definition of the subject-matter of this claim unclear (Article 6 PCT).

6. The chemical structure of the compound "hydroethyliden (1,1 diphosphate) acid" is not clear.

7. Present claim 15 cannot depend on claim 14, since claim 14 does not define the presence of a "phosphate".

8. The terms "deoxygenating compound" and "reaction oxidation (or oxidation reaction) reverting compound" are unusual in the art.

The term "deoxygenating compound" has been understood to be a compound that diminishes the oxygen solubility in the medium.
The term "reaction oxidation (or oxidation reaction) reverting compound" has been understood to be a reducing agent.

PATENT COOPERATION TREA

From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

To:
DANNEMANN, SIEMSEN, BIGLER &
IPANEMA MOREIRA
Rua Marques de Olinda 70
Caixa Postal 2142
22251-040- Rio de Janeiro - RJ
BRAZIL

Date of mailing *(day/month/year)* 18/12/2000	
Applicant's or agent's file reference PE-3933	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/BR 00/00077	International filing date *(day/month/year)* 14/07/2000

Applicant

INDUSTRIA E COMERCIO DE COSMETICOS NATURA LTDA.

1. [X] The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:
The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Fascimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

[ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

[ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the pr scribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because th y are not bound by Chapter II.

Name and mailing address of the International Searching Authority	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Joannes Vergoosen

Form PCT/ISA/220 (July 1998)

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREA

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.
PE-3933		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/BR 00/ 00077	14/07/2000	16/07/1999

Applicant

INDUSTRIA E COMERCIO DE COSMETICOS NATURA LTDA.

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readble form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

TWO-COMPONENT COMPOSITION FOR COSMETIC OR PHARMACEUTICAL USE

5. With regard to the **abstract**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to a biphasic composition for cosmetic or pharmaceutical use comprising antioxidants and beneficial compounds for the skin, such as moisturizers and immunomodulators.
The composition comprises ascorbic acid as the antioxidant compound and ceramides as the selected moisturing agent and betaglycane as the immunomodulator, presenting a low potential risk for sensitization and having effective antioxidant action, in addition to an outstanding sensitive effect.

INTERNATIONAL SEARCH REPORT

[redacted]national Application No
PCT/BR 00/00077

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/00 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 804 168 A (MURAD HOWARD) 8 September 1998 (1998-09-08) column 3, line 30-64 column 4, line 10-12 column 5, line 39-45 column 13, line 26-63 column 15, line 55 -column 16, line 23 claim 1 --- -/--	1,3,8, 12,13

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 December 2000	18/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bazzanini, R

2

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
PCT/BR 00/00077

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 33439 A (ROBERTS RICHARD L ;GREENE JAMES A (US); SHAKLEE CORP (US); SIDDIQU) 8 July 1999 (1999-07-08) page 6, line 3-26 page 8, line 10-17 page 10, line 9-14 page 14, line 30 -page 15, line 10 examples 5,6,11,12 page 31, line 13-25 page 32, line 12-18 claims 1-5	1,3,8, 11-13
X	US 5 902 591 A (HERSTEIN MORRIS) 11 May 1999 (1999-05-11) column 2, line 66 -column 3, line 6 column 3, line 15-23 column 4, line 40-46 column 6, line 54-67 column 7, line 48-50 column 11, line 65 -column 13, line 11	1,3,8,12
A	US 5 626 883 A (PAUL STEPHEN M) 6 May 1997 (1997-05-06) column 2, line 50 -column 3, line 10 column 5, line 55-58 column 7, line 61-67 column 8, line 20-23	1-21
A	US 5 094 783 A (BROUILLETTE WAYNE J ET AL) 10 March 1992 (1992-03-10) column 1, line 56-60 column 2, line 60-63	1-21

2

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims 1,3,6,8-21 have been searched incompletely.

Present claims 1,3,6,8-21 relate to an extremely large number of possible compounds due to the use of very generic words such as "biphasic", "antioxidant", "moisturizer", "immunomodulator" (claim 1) and "deoxygenating compound" (claim 8). Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds specifically mentioned in the description and in the claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/BR 00/00077

Box I Observations wher certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.: ,
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Pr test

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/BR 00/00077

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5804168 A	08-09-1998	NONE	
WO 9933439 A	08-07-1999	US 6036946 A	14-03-2000
		US 6015548 A	18-01-2000
		AU 1944599 A	19-07-1999
		EP 1047392 A	02-11-2000
US 5902591 A	11-05-1999	EP 1037585 A	27-09-2000
		WO 9843598 A	08-10-1998
US 5626883 A	06-05-1997	AU 2384695 A	10-11-1995
		WO 9528084 A	26-10-1995
US 5094783 A	10-03-1992	AU 8197091 A	23-01-1992
		WO 9200360 A	09-01-1992

PATENT COOPERATION TREATY

From the:
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

DANNEMANN, SIEMSEN, BIGLER & IPANEM
A MOREIRA
Rua Marques de Olinda, 70
Caixa Postal 2142
CEP-22251-040 Rio de Janeiro, RJ
BRESIL

PCT

WRITTEN OPINION

(PCT Rule 66) 01

Date of mailing *(day/month/year)*	31.07.2001
Applicant's or agent's file reference: PE-3933	**REPLY DUE** **within 1 month(s) and 15 days** from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/BR00/00077	14/07/2000	16/07/1999

International Patent Classification (IPC) or both national classification and IPC

A61K7/00

Applicant

INDUSTRIA E COMERCIO DE COSMETICOS NATURA LTDA.

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

I	☒	Basis of the opinion
II	☐	Priority
III	☐	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
IV	☐	Lack of unity of invention
V	☒	Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
VI	☐	Certain document cited
VII	☒	Certain defects in the international application
VIII	☒	Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also: For an additional opportunity to submit amendments, see Rule 66.4. For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis. For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 16/11/2001.

Name and mailing address of the international preliminary examining authority:
European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer / Examiner
Pregetter, M

Formalities officer (incl. extension of time limits)
Longo, E
Telephone No. +49 89 2399 8141

I. Basis of the opinion

1. With regard to the **elements** of the international application (Replacement *sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed"*):

   Description, pages:

   1-12 as originally filed

   Claims, No.:

   1-21 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	1-21
Inventive step (IS)	Claims	
Industrial applicability (IA)	Claims	

2. Citations and explanations
   see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
se separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statem nt

1. Reference is made to the following documents:

   D1: US-A-5 804 168 (MURAD HOWARD) 8 September 1998 (1998-09-08)
   D2: WO 99 33439 A (ROBERTS RICHARD L ;GREENE JAMES A (US); SHAKLEE CORP (US); SIDDIQU) 8 July 1999 (1999-07-08)
   D3: US-A-5 902 591 (HERSTEIN MORRIS) 11 May 1999 (1999-05-11)

2. The subject-matter of present claim 1 is not novel according to Article 33(2) PCT.
   Document D1 discloses aqueous emulsions comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (propylene glycol and/or butylene glycol), a metallic ions sequestering compound (EDTA), and, in the dispersed phase, immunomodulators (retinyl and/or ascorbyl palmitates) and moisturizers/emollients (col.13, l.25-64 and col.15, l.55-col.16, l.24).
   D2 describes an oil-in-water formulation comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (the most common humectants are glycols), a metallic ions sequestering agent, and, in the dispersed phase, immunomodulator (beta glucan) and moisturizers/emollients. Proanthocyanidins in the form of grape seed extract are also present (e.g. example 6).

3. The subject-matter of present claim 8 is not novel according to Article 33(2) PCT.
   D2 describes an oil-in-water formulation comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (the most common humectants are glycols), a metallic ions sequestering agent, a reducing agent (superoxide dismutase), and, in the dispersed phase, immunomodulator (beta glucan) and moisturizers/emollients (e.g. example 6).
   D3 discloses a mixture of 5% powdered ascorbic acid with 95% of an emulsion resulting in dissolving the ascorbic acid in the aqueous phase of said emulsion. The resulting aqueous phase comprises the ascorbic acid (antioxidant), a

deoxygenating agent (butylene glycol), a metallic ions sequestering compound (EDTA) and a reducing agent (superoxide dismutase).

4. With regard to the dependent claims, it is noted that a positive opinion can only be given, if dependent claims refer to independent claims that meet the requirements of the PCT.
Furthermore, the following has to be noted:
The use of a substance in certain percentages can only be considered to involve an inventive step, if it can be clearly shown that said percentages are unusual in the art and lead to a surprising effect.
The use of a specific immunomodulator, reducing agent, sequestering agent, ... can only be considered to involve an inventive step, if such a use is unusual in the art and leads to a surprising effect. However, the combination of specific compounds in specific percentages is very often not suggested by the prior art.

5. In order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter whether they concern amendments by addition, replacement or deletion, and to indicate the passages of the application as filed on which these amendments are based (see also Rule 66.8(a) PCT).
In case of non-compliance, said amendments cannot be taken into account when establishing the international preliminary examination report.

Re Item VII
Certain defects in the international application

1. According to Rule 10(f) PCT the beginning of a decimal fraction has to be marked by a period.

2. The description is not in conformity with claims 7-21 as required by Rule 5.1(a)(iii) PCT.

Re Item VIII
Certain observations on the international application

1. The term "biphasic" used throughout the claims is vague and unclear and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of the claims unclear (Article 6 PCT).
   The term "biphasic" can relate to either solid/liquid or liquid/gaseous compositions (or others) or to hydrophilic/hydrophobic compositions such as dispersions (or very often emulsions). Furthermore, according to the statement on p.3, l.29-p.4, l.4, the term "biphasic" can also refer to two phases which are separately packaged, although the term "phases" does not seem to be a very fitting term for two solutions which are separately packaged.
   Present claim 8 does not even define any second "phase".
   For the purpose of preliminary examination all possibilities have to be taken into consideration.

2. The term "preferably" does not limit the scope of a claim in any way.

3. Present claim 3 cannot depend on claim 2, because the range of 0.0001 to 0.001% by weight is not included in the range given in claim 2 (Article 6 PCT).

4. The use of parenthesis and abbreviations in claims leads to a lack of clarity (Article 6 PCT).

5. The term "Dequest" employed in claim 7 and appearing to be a registered trade mark has no precise meaning as it is not internationally accepted as a standard descriptive term, thereby rendering the definition of the subject-matter of this claim unclear (Article 6 PCT).

6. The chemical structure of the compound "hydroethyliden (1,1 diphosphate) acid" is not clear.

7. Present claim 15 cannot depend on claim 14, since claim 14 does not define the presence of a "phosphate".

8. The terms "deoxygenating compound" and "reaction oxidation (or oxidation reaction) reverting compound" are unusual in the art.

The term "deoxygenating compound" has been understood to be a compound that diminishes the oxygen solubility in the medium.
The term "reaction oxidation (or oxidation reaction) reverting compound" has been understood to be a reducing agent.

PCT

REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No. / 0 0077

International Filing Date 19 JUL 2000 00

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference *(if desired) (12 characters maximum)* PE-3933

Box No. I TITLE OF INVENTION

"BIPHASIC COMPOSITION FOR COSMETIC OR PHARMACEUTICAL USE"

Box No. II APPLICANT

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

INDÚSTRIA E COMÉRCIO DE COSMÉTICOS
NATURA LTDA.
Rodovia Regis Bittencourt S/N
KM 293
06850 - Itapecerica da Serra - SP
Brazil

☐ This person is also inventor.

Telephone No. (11) 7940-1311

Facsimile No. (11) 7940-1094

Teleprinter No.

State *(that is, country)* of nationality: BR

State *(that is, country)* of residence: BR

This person is applicant for the purposes of: ☐ all designated States ☒ all designated States except the United States of America ☐ the United States of America only ☐ the States indicated in the Supplemental Box

Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

ALCANTARA MARTINS ZUCCHETTI, ROBERTO
Rua Serra do Japi, 242, apto. 23B
Tatuapé
São Paulo - SP
Brazil

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: BR

State *(that is, country)* of residence: BR

This person is applicant for the purposes of: ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as: ☒ agent ☐ common representative

Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*

DANNEMANN, SIEMSEN, BIGLER & IPANEMA MOREIRA
Caixa Postal 2142
Rua Marques de Olinda, 70
22251-040 - Rio de Janeiro - RJ
Brazil

Telephone No. (21) 553.1811

Facsimile No. (21) 553.1812
553.1813

Teleprinter No.

☐ **Address for correspondence:** Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

Sheet No. 02

Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request.

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

VILLA NOVA SILVA, LUCIANA
Rua Américo Alves Pereira Filho, 564
Morumbi
São Paulo, SP
Brazil

This person is:
- [ ] applicant only
- [x] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: BR

State *(that is, country)* of residence: BR

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [x] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

CHITARRA SOUZA, SIMONI
Rua Estela, 22, apto. 331
Paraíso
São Paulo - SP
Brazil

This person is:
- [ ] applicant only
- [x] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: BR

State *(that is, country)* of residence: BR

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [x] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

FANAN, SIMONE
Rua Rafael Sampaio, 500
Campinas, SP
Brazil

This person is:
- [ ] applicant only
- [x] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: BR

State *(that is, country)* of residence: BR

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [x] the United States of America only
- [ ] the States indicated in the Supplemental Box

Name and address: *(Family name followed by given name: for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)*

GESZTESI, JEAN-LUC
Rua General Jardim, 840 - 5º andar
São Paulo - SP
Brazil

This person is:
- [ ] applicant only
- [x] applicant and inventor
- [ ] inventor only *(If this check-box is marked, do not fill in below.)*

State *(that is, country)* of nationality: BR

State *(that is, country)* of residence: BR

This person is applicant for the purposes of:
- [ ] all designated States
- [ ] all designated States except the United States of America
- [x] the United States of America only
- [ ]

[x] Further applicants and/or (further) inventors are indicated on an ther continuation sheet.

Supplemental Box *If the Supplemental Box is not used, this sheet should not be included in the request.*

1. If, in any of the Boxes, the space is insufficient to furnish all the information, in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient, in particular:

(i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available: in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below;

(ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;

(iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America: in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;

(iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents: in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;

(v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "continuation" or "continuation-in-part": in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;

(vi) if, in Box No. VI, there are more than three earlier applications whose priority is claimed: in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI;

(vii) if, in Box No. VI, the earlier application is an ARIPO application: in such case, write "Continuation of Box No. VI", specify the number of the item corresponding to that earlier application and indicate at least one country party to the Paris Convention for the Protection of Industrial Property or one Member of the World Trade Organization for which that earlier application was filed.

2. If, with regard to the precautionary designation statement contained in Box No. V, the applicant wishes to exclude any State(s) from the scope of that statement: in such case, write "Designation(s) excluded from precautionary designation statement" and indicate the name or two-letter code of each State so excluded.

3. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty: in such case, write "Statement concerning non-prejudicial disclosures or exceptions to lack of novelty" and furnish that statement below.

Continuation of Box III

MARTINS MATHEUS, LUIZ GUSTAVO
Brazilian
Rua Winston Churchil, 400, Jardim São Caetano
São Caetano do Sul, SP
Brazil

This person is applicant and inventor for the purposes of the United States of America only.

POMMEZ, PHILIPPE JOSEPH
Canadian
Rua Alceu Maynard Araújo, 433, Bloco B, apto. 21
São Paulo - SP
Brazil

This person is applicant and inventor for the purposes of the United States only.

Box No.V DESIGNATION OF STATES

The following designations are hereby made under Rule 4.9(a) *(mark the applicable check-boxes; at least one must be marked)*:

Regional Patent

☐ **AP** **ARIPO Patent:** GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT

☐ **EA** **Eurasian Patent:** AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT

☒ **EP** **European Patent:** AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT

☐ **OA** **OAPI Patent:** BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT *(if other kind of protection or treatment desired, specify on dotted line)* .....

National Patent *(if other kind of protection or treatment desired, specify on dotted line)*:

☐ **AE** United Arab Emirates
☐ **AL** Albania .....
☐ **AM** Armenia .....
☐ **AT** Austria .....
☐ **AU** Australia .....
☐ **AZ** Azerbaijan
☐ **BA** Bosnia and Herzegovina .....
☐ **BB** Barbados
☐ **BG** Bulgaria .....
☐ **BR** Brazil .....
☐ **BY** Belarus .....
☒ **CA** Canada
☐ **CH and LI** Switzerland and Liechtenstein
☐ **CN** China .....
☐ **CR** Costa Rica .....
☐ **CU** Cuba .....
☐ **CZ** Czech Republic .....
☐ **DE** Germany .....
☐ **DK** Denmark .....
☐ **DM** Dominica
☐ **EE** Estonia .....
☐ **ES** Spain .....
☐ **FI** Finland .....
☐ **GB** United Kingdom
☐ **GD** Grenada
☐ **GE** Georgia .....
☐ **GH** Ghana .....
☐ **GM** Gambia
☐ **HR** Croatia .....
☐ **HU** Hungary .....
☐ **ID** Indonesia
☐ **IL** Israel .....
☐ **IN** India .....
☐ **IS** Iceland
☒ **JP** Japan .....
☐ **KE** Kenya .....
☐ **KG** Kyrgyzstan .....
☐ **KP** Democratic People's Republic of Korea .....
☐ **KR** Republic of Korea .....
☐ **KZ** Kazakhstan .....
☐ **LC** Saint Lucia
☐ **LK** Sri Lanka
☐ **LR** Liberia
☐ **LS** Lesotho .....
☐ **LT** Lithuania
☐ **LU** Luxembourg
☐ **LV** Latvia
☐ **MA** Morocco .....
☐ **MD** Republic of Moldova .....
☐ **MG** Madagascar .....
☐ **MK** The former Yugoslav Republic of Macedonia .....
☐ **MN** Mongolia
☐ **MW** Malawi .....
☐ **MX** Mexico .....
☐ **NO** Norway
☐ **NZ** New Zealand .....
☐ **PL** Poland .....
☐ **PT** Portugal .....
☐ **RO** Romania
☐ **RU** Russian Federation .....
☐ **SD** Sudan
☐ **SE** Sweden
☐ **SG** Singapore
☐ **SI** Slovenia .....
☐ **SK** Slovakia .....
☐ **SL** Sierra Leone .....
☐ **TJ** Tajikistan .....
☐ **TM** Turkmenistan .....
☐ **TR** Turkey .....
☐ **TT** Trinidad and Tobago .....
☐ **TZ** United Republic of Tanzania
☐ **UA** Ukraine .....
☐ **UG** Uganda .....
☒ **US** United States of America .....
☐ **UZ** Uzbekistan .....
☐ **VN** Viet Nam .....
☐ **YU** Yugoslavia .....
☐ **ZA** South Africa .....
☐ **ZW** Zimbabwe .....

Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:

☐ .....
☐ .....

Precautionary Designation Statement: In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. *(Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)*

Box No. VI PRIORITY CLAIM ☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is: national application: country	regional application:* regional Office	international application: receiving Office
item (1) 16 July 1999 (16.07.99)	PI 9902972-3	BR		
item (2)				
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) *(only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office)* identified above as item(s): 1

** Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.*

Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) *(if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):*
ISA/ EPO

Request to use results of earlier search; reference to that search *(if an earlier search has been carried out by or requested from the International Searching Authority):*
Date *(day/month/year)* Number Country *(or regional Office)*

Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following **number of sheets**:

request	5
description (excluding sequence listing part)	12
	3
claims	
abstract	1
drawings	-
sequence listing part of description	-
Total number of sheets	21

This international application is **accompanied by** the item(s) marked below:

1. ☒ fee calculation sheet
2. ☒ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other *(specify)*: inventors' assignment

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: English

Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

Dannemann, Siemsen, Bigler & Ipanema Moreira

For receiving Office use only

1. Date of actual receipt of the purported international application: 14 JUL 2000
2. Drawings: ☐ received: ☐ not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:
4. Date of timely receipt of the required corrections under PCT Article 11(2):
5. International Searching Authority (if two or more are competent): ISA/
6. ☐ Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

This sheet is not part of and does not count as a sheet of the international application.

PCT

FEE CALCULATION SHEET

Annex t the Request

For receiving Office use only

International application No.

Date stamp of the receiving Office

Applicant's or agent's file reference PE-3933

Applicant

INDÚSTRIA E COMÉRCIO DE COMÉSTICOS NATURA LTDA. et al

CALCULATION OF PRESCRIBED FEES

1. TRANSMITTAL FEE . . . . . 236,00 T

2. SEARCH FEE DEM 462,07 x 0.86906 . . . . . 401,56 S

International search to be carried out by EPO

(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

Basic Fee

The international application contains 21 sheets.

first 30 sheets CHF 650 x 1,09564 . . . 712,16 b1

___ (remaining sheets) x ___ (additional amount) = - b2

Add amounts entered at b1 and b2 and enter total at B . . . . 712,16 B

Designation Fees

The international application contains 4 designations.

4 (number of designation fees payable *(maximum 8)*) x CHF 140 x 1.09564 (amount of designation fee) = 613,55 D

Add amounts entered at B and D and enter total at I . . . . . 1.325,71 I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT *(if applicable)* . . . . . 75,00 P

5. TOTAL FEES PAYABLE . . . . . R$ 2.038,27 TOTAL

Add amounts entered at T, S, I and P, and enter total in the TOTAL box

☐ The designation fees are not paid at this time.

MODE OF PAYMENT

☐ authorization to charge deposit account (see below)	☐ bank draft	☐ coupons
☐ cheque	☒ cash	☐ other *(specify)*:
☐ postal money order	☐ revenue stamps	

DEPOSIT ACCOUNT AUTHORIZATION *(this mode of payment may not be available at all receiving Offices)*

The RO/ _____

☐ is hereby authorized to charge the total fees indicated ab ve to my deposit account.

☐ *(this check-box may be marked only if the conditions for deposit accounts of the receiving Office so permit)* is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated ab ve to my dep sit account.

☐ is hereby authorized to charge the fee for preparati n and transmittal f the priority d cument t the International Bureau of WIPO to my dep sit acc unt.

Deposit Account No. | Date *(day/month/year)* | Signature

TENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION** see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
PE-3933		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/BR 00/ 00077	14/07/2000	16/07/1999
Applicant		
INDUSTRIA E COMERCIO DE COSMETICOS NATURA LTDA.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 4 sheets.

☐ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**

   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

   b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readble form.

   ☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title,**

   ☐ the text is approved as submitted by the applicant.

   ☒ the text has been established by this Authority to read as follows:

   TWO-COMPONENT COMPOSITION FOR COSMETIC OR PHARMACEUTICAL USE

5. With regard to the **abstract,**

   ☐ the text is approved as submitted by the applicant.

   ☒ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

   ☐ as suggested by the applicant.

   ☐ because the applicant failed to suggest a figure.

   ☐ because this figure better characterizes the invention.

   ☒ None of the figures.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims 1,3,6,8-21 have been searched incompletely.

Present claims 1,3,6,8-21 relate to an extremely large number of possible compounds due to the use of very generic words such as "biphasic", "antioxidant", "moisturizer", "immunomodulator" (claim 1) and "deoxygenating compound" (claim 8). Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds specifically mentioned in the description and in the claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

B x III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

The present invention relates to a biphasic composition for cosmetic or pharmaceutical use comprising antioxidants and beneficial compounds for the skin, such as moisturizers and immunomodulators.
The composition comprises ascorbic acid as the antioxidant compound and ceramides as the selected moisturing agent and betaglycane as the immunomodulator, presenting a low potential risk for sensitization and having effective antioxidant action, in addition to an outstanding sensitive effect.

INTERNATIONAL SEARCH REPORT

International Application No
P[redacted]R 00/00077

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/00 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 804 168 A (MURAD HOWARD) 8 September 1998 (1998-09-08) column 3, line 30-64 column 4, line 10-12 column 5, line 39-45 column 13, line 26-63 column 15, line 55 -column 16, line 23 claim 1 --- -/--	1,3,8, 12,13

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 December 2000	18/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bazzanini, R

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Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

International Application No
[redacted]BR 00/00077

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 33439 A (ROBERTS RICHARD L ;GREENE JAMES A (US); SHAKLEE CORP (US); SIDDIQU) 8 July 1999 (1999-07-08) page 6, line 3-26 page 8, line 10-17 page 10, line 9-14 page 14, line 30 -page 15, line 10 examples 5,6,11,12 page 31, line 13-25 page 32, line 12-18 claims 1-5	1,3,8, 11-13
X	US 5 902 591 A (HERSTEIN MORRIS) 11 May 1999 (1999-05-11) column 2, line 66 -column 3, line 6 column 3, line 15-23 column 4, line 40-46 column 6, line 54-67 column 7, line 48-50 column 11, line 65 -column 13, line 11	1,3,8,12
A	US 5 626 883 A (PAUL STEPHEN M) 6 May 1997 (1997-05-06) column 2, line 50 -column 3, line 10 column 5, line 55-58 column 7, line 61-67 column 8, line 20-23	1-21
A	US 5 094 783 A (BROUILLETTE WAYNE J ET AL) 10 March 1992 (1992-03-10) column 1, line 56-60 column 2, line 60-63	1-21

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/BR 00/00077

Patent document cited in search report		Publication date	Patent family member(s)		Publication date
US 5804168	A	08-09-1998	NONE		
WO 9933439	A	08-07-1999	US	6036946 A	14-03-2000
			US	6015548 A	18-01-2000
			AU	1944599 A	19-07-1999
			EP	1047392 A	02-11-2000
US 5902591	A	11-05-1999	EP	1037585 A	27-09-2000
			WO	9843598 A	08-10-1998
US 5626883	A	06-05-1997	AU	2384695 A	10-11-1995
			WO	9528084 A	26-10-1995
US 5094783	A	10-03-1992	AU	8197091 A	23-01-1992
			WO	9200360 A	09-01-1992

PATENT COOPERATION TREATY

VLP

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

DANNEMANN, SIEMSEN, BIGLER & IPANEM
A MOREIRA
Rua Marques de Olinda, 70
Caixa Postal 2142
CEP-22251-040 Rio de Janeiro, RJ
BRESIL

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	19.10.2001
Applicant's or agent's file reference	IMPORTANT NOTIFICATION
PE-3933	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/BR00/00077	14/07/2000	16/07/1999

Applicant
INDUSTRIA E COMERCIO DE COSMETICOS NATURA LTDA.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Götz, K Tel.+49 89 2399-7381

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PE-3933		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/BR00/00077	14/07/2000	16/07/1999
International Patent Classification (IPC) or national classification and IPC A61K7/00		
Applicant INDUSTRIA E COMERCIO DE COSMETICOS NATURA LTDA.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 15 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15/02/2001	19.10.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Pregetter, M Telephone No. +49 89 2399 8719

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BR00/00077

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-12	as received on	14/09/2001	with letter of	13/09/2001

Claims, No.:

1-21	as received on	14/09/2001	with letter of	13/09/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2,4,5,7,14-16
	No:	Claims	1,3,6,8-13,17-21
Inventive step (IS)	Yes:	Claims	2,4,5,7,14-16
	No:	Claims	1,3,6,8-13,17-21
Industrial applicability (IA)	Yes:	Claims	1-21
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

R Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: US-A-5 804 168 (MURAD HOWARD) 8 September 1998 (1998-09-08)
   D2: WO 99 33439 A (ROBERTS RICHARD L ;GREENE JAMES A (US); SHAKLEE CORP (US); SIDDIQU) 8 July 1999 (1999-07-08)
   D3: US-A-5 902 591 (HERSTEIN MORRIS) 11 May 1999 (1999-05-11)
   D4: US-A-5 626 883 (PAUL STEPHEN M) 6 May 1997 (1997-05-06)
   D5: US-A-5 094 783 (BROUILLETTE WAYNE J ET AL) 10 March 1992 (1992-03-10)

2. The subject-matter of present claim 1 is not novel according to Article 33(2) PCT. Document D1 discloses aqueous emulsions comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (propylene glycol and/or butylene glycol), a metallic ions sequestering compound (EDTA), and, in the dispersed phase, immunomodulators (retinyl and/or ascorbyl palmitates) and moisturizers/emollients (col.13, l.25-64 and col.15, l.55-col.16, l.24).
   D2 describes an oil-in-water formulation comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (the most common humectants are glycols), a metallic ions sequestering agent, and, in the dispersed phase, immunomodulator (beta glucan) and moisturizers/emollients. Proanthocyanidins in the form of grape seed extract are also present (e.g. example 6).

3. The subject-matter of present claim 8 is not novel according to Article 33(2) PCT. D2 describes an oil-in-water formulation comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (the most common humectants are glycols), a metallic ions sequestering agent, a reducing agent (superoxide dismutase), and, in the dispersed phase, immunomodulator (beta glucan) and moisturizers/emollients (e.g. example 6).

4. None of the documents cited in the search report discloses the combination of ceramides as moisturizer and betaglycan as immunomodulator in a composition comprising an antioxidant.
Since ceramides are not even mentioned in any of the documents cited in the search report, such a combination is furthermore not suggested.
Consequently the subject-matter of claims 2,4 and 5 is considered to be novel and inventive according to Articles 33(2) and (3) PCT.

5. None of the documents cited in the search report suggest to use phosphorous based sequestering agents.
Consequently the subject-matter of claims 7 and 14-16 is considered to be novel and inventive according to Articles 33(2) and (3) PCT.

6. The dependent claims 3, 6, 9-13, 17-21 do not contain any features which, in combination with the features of any claim to which they refer, might establish novelty and an inventive step over D1-D5 (Articles 33(2) and 33(3) PCT).

Re Item VIII
Certain observations on the international application

1. The subject-matter of present claims 1 and 8 is defined by using the term "comprise". This term "comprise" does not exclude the presence of further compounds.

2. The term "phase" can be interpreted in at least two different ways. Firstly, it can be construed in the sense of "liquid phase", "solid phase" or "gaseous phase", secondly it can be seen to mean "hydrophilic phase" versus "hydrophobic phase" and thirdly it can be interpreted to mean several "physically separated entities". For the purpose of examination, all possibilities have to be taken into consideration.

Title : "COMPOSITION FOR COSMETIC OR PHARMACEUTICAL USE".

Field of the Invention

The present invention relates to an aqueous composition especially improved for cosmetic and pharmaceutical compositions, comprising antioxidant compounds and other beneficial compounds for the skin as moisturizers and immunomodulators.

Prior Art

Cosmetic and pharmaceutical compositions including antioxidants are very well known for improving the skin aspect, e.g., preventing marks from showing on the skin, such as wrinkles, flaccidity, spots, or to treat mild problems such as irritations and other mild diseases.

In this kind of composition, antioxidant compounds are commonly used, such as levogyrous ascorbic acid (LAA), popularly known as "Vitamin C" and proanthocyanidins (OPC) because, among other characteristics, they act against the free radicals which accelerate the aging process and the cellular degeneration.

Said compositions lack, however, the supplying of a substantial improvement in the general quality of the skin, because they normally approach one or another problem singly. In addition, if on the one hand antioxidants bring improvement benefits for the skin or help to the cells health, on the other hand they can cause sensitivities to certain people.

When sensitivities occur, they can be attributed to the nature of certain antioxidants or to the concentrations required to obtain the desired benefits, which can vary from 5 to 10% or even 20% by weight. Lower antioxidants concentrations might not be potentially irritant, however, the effects they produce are below what would be desirable.

Still in that respect, compositions comprising antioxidants derivatives are very used. Only as an example, LAA esters can be used instead ascorbic acid in its molecular form (LAA). This kind of composition gives rise, until nowadays, to a great discussion among scientists, as for its effectiveness.

One fact that reinforces the theory of a better effectiveness of the antioxidants in their original form is the quantity of studies and publications related to the stabilization of such compounds. Examples of these studies are described in Brazilian pat nt

applications PI 9704418-0 and PI 9704728-7 and in the prior art references mentioned therein, all of them dedicated to the LAA stabilization.

The OPC's, in their turn, are known by those skilled in the art from many already published works. One of these relates to the patent granted in the United States under number US 4,698,360, to Masquelier, Jacque.

In that patent, anti-free radicals effects provided by such compounds are discussed, with therapeutic indications, including by oral, intravenous and topic route.

Compounds exclusively comprising OPC can bring beneficial effects to the user, however, they show a limited action and benefits scope.

In a further evolution, the patent granted in the United States to Lerner, Sheldom under number US 5,470,874 describes compositions comprising as main actives associated OPC's as a mixture to the ascorbic acid in its molecular form and derivatives as the ascorbyl palmitate.

As it can be noted from this last document mentioned, the composition taught therein to obtain a set of benefits for the skin is extremely complex, having always more than ten ingredients.

In addition to the composition complexity, the benefit scope provided by such composition is limited. Although the number of benefits counted is larger than the one described in US 4,698,360, these could bring some disadvantages.

A first disadvantage is a result of the high LAA contents used, always above 10%, sometimes reaching 25%, which cause a greater skin exfoliation and an uncomfortable sensation (burning), sometimes causing a contact allergy or even making the skin more sensitive to inflammations.

In addition, these high contents provide a very acid pH that causes a lower effectiveness in the complexing activity of the preservative included therein, namely EDTA, which leads to a faster degradation of the LAA.

Summarizing, the aggressive condition provided by the combination of compounds disclosed in the above patent becomes damaging also because it is free from any present or associated entity capable of reducing such aggressiveness in such a way to supply a comfortable product for the user.

Therefore, it is an objective of the present invention to provide a composition for cosmetic or pharmaceutical use which supplies a wide range of benefits, and while in

use, provides to the user a solution of commitment between the expected effectiveness, due to the presence of antioxidants, and the comfort for the user, with superior results when compared with the known compositions as far as improvement of skin quality are concerned.

Summary of the Invention

The present invention relates to a composition for cosmetic or pharmaceutical use wherein it comprises a first phase which contains an antioxidant compound in an aqueous medium, and a second phase which comprises a moisturizer compound and an immunomodulator, and wherein the proportion of said first to the second phase is from 6:1 to 14:1.

Detailed Description of the Invention

It was surprisingly found by the present inventors that a composition for cosmetic or pharmaceutical use comprising, at least one antioxidant in a first phase and, in a second phase, at least one moisturizing agent and one immunomodulator, wherein the application proportion between the first and the second phases ranges from 6:1 to 14:1, provides a wide range of benefits and, while in use, provides to the user both effectiveness, in view of the presence of antioxidants, and the comfort for the user, i.e., low potential of irritation, with superior results when compared with compositions known from the prior art as far as improvement of skin quality is concerned.

Antioxidants useful for the present invention should be understood as compounds or mixture of compounds which have properties against the free radicals present in the body, especially in the skin.

Moisturizing agents useful for the present invention are compounds or mixtures of compounds able to restructure the skin barrier.

Immunomodulators are understood as any compound or mixture of compounds able to reinforce the skin immunological system.

According to a preferred embodiment of the present invention, the composition for cosmetic or pharmaceutical use comprises two different phases, which, due to their nature, can be conveniently packed in only one dispenser. Each phase, however, must be present in sealed compartments within said dispenser, which prevent contact between the phases prior to the moment of use, when they are simultaneously dispensed from said dispenser, e.g., due to incompatibility between both of them, which

could lead to the unstableness or degradation of the compounds as time goes by. An example of this kind of package is described in patent document WO 97/27841.

According to the above embodiment of the invention, the composition comprises in a first dispenser compartment, a first phase containing an aqueous composition comprising an antioxidant, preferably ascorbic acid, present at a concentration from 1 to 30% and, in a second phase, a moisturizer such as ceramides, from 0.5 to 3.0%, and the sodic betaglycan carboxyl immunomodulator, also known as betaglycane, present in a content from 0.5 to 3.0%, the application proportion between said first and second phases being from 6:1 to 14:1. All percentages set forth above are in weight relative to the total weight of the composition of each phase.

In a preferred embodiment of the present invention, such composition comprises in a first dispenser compartment, a first phase in which an aqueous composition is present, comprising a plurality of antioxidants such as ascorbic acid, present at a percentage from 1 to 20%, and OPC's present from about 0.001 to 2.2% and, in a second phase, a moisturizer such as ceramides, preferably ceramides contained in a liquid crystal emulsion, also called lamellar ceramide, in a content from 0.5 to 3.0%, associated to the sodic betaglycan carboxyl immunomodulator, also known as betaglycane, present in a content from 0.5 to 3.0%, the application proportion between said first and second phases being from 6:1 to 14:1, preferably, between 12:1 to 8:1. All the percentages mentioned above are in weight relative to the total weight of the composition of each phase.

It was found that the use of compositions as described above improves strength and natural protection of the skin against external aggressions due to the association of the restructuring effect of the skin lipidic barrier by the lamellar ceramides with the reinforcement effect of the skin immunological system provided by the betaglycanes.

In an even more preferred embodiment of the invention, the composition comprises a first phase in a first dispenser compartment, where an aqueous composition is present comprising a plurality of antioxidants such as the ascorbic acid present at a percentage from 1 to 20%, preferably between 5 and 18%, and OPC's, present from about 0.001 to 2.2%, preferably between 0.01 and 1.7% and, in a second phase, a moisturizer such as ceramides, preferably ceramides contained in a liquid crystal emulsion, also called lamellar ceramide, in a range from 0.5 to 3.0%, preferably

b tween 1.5 to 2.5%, associated to sodic betaglycan carboxyl the immunomodulator, also known as betaglycane, which is present in a content from 0.5 to 3.0%, preferably between 1.5 to 2.5%, the application proportion between said first and second phases being from 6:1 to 14:1, preferably, between 12:1 to 8:1, and most preferably, around 11:1. All the percentages above mentioned are in weight relative to the total weight of the composition of each phase.

It has been observed that an adequate proportion between the first phase and the second phase is at about 6:1 to 14:1, preferably between 12:1 to 8:1 and, most preferably, around 11:1. The association of the two phases recovers the skin vitality and imparts an improvement of the skin strength and natural protection.

In vitro studies carried out by the inventors showed that the effects obtained with the composition of the invention can be improved when the ascorbic acid is the levogyrous ascorbic acid (LAA), present within a selected concentration range.

Several essays were carried out by the inventors with the objective of determining in which concentration range the levogyrous ascorbic acid (LAA) has antioxidant and pro-oxidant activity and the results showed that LAA pro-oxidant action occurs in a concentration range between 0.005% and 0.01% while the antioxidant action occurs in ranges between 0.0001% and 0.001% and between 1 and 10%. In these essays, it was also observed that at concentrations between 0.1 and 0.4%, preferably around 0.3% of OPC's associated to the LAA in an aqueous medium, the pro-oxidant effect of the LAA present in the percentage range where it acts as pro-oxidant is inhibited. This conclusion derives from the observation that, in this essay, the deoxyribose degradation decreases 78%.

Advantageously, said first phase contains the antioxidants in their molecular stable or original form (without degradation) but their salts and esters could also be used, certainly leading to good results. In this last case where salts, esters or polymerized antioxidants are to be used, it is believed that the separation between the first and the second phase prior to use could, in some particular cases, be unnecessary. In addition, other compounds can be easily added to the above described components without representing much difficulty for those skilled in the art. Just as an example, such compounds include fragrances, thickeners, and moisteners or other moisturizers.

In another even more advantageous embodiment, the composition of the invention comprises, in a first phase, at least one antioxidant compound in an aqueous medium, at least one deoxygenating compound, and at least one metallic ions sequestering compound, and at least one reducing agent.

It has been now surprisingly found by the present inventors that the association of at least one antioxidant compound, in an aqueous medium, with a reducing agent, without considering the oxidation reaction stechiometry, a deoxygenating agent and a metallic ions sequestering compounds, makes it possible to improve the performance and the synergy of such first phase with the second phase of said composition, even when using ascorbic acid contents lower than 10%, without impairing the composition performance, as it will be further described in detail.

For the purposes of the present invention, some terms definitions are presented below.

A reducing agent is any compound or mixture of compounds which shows a oxidation potential greater than the oxidation potential of the antioxidant to be stabilized so that the antioxidant subcompounds that are generated return to the original antioxidant form, that is to say, to its molecular form.

Concerning the deoxygenating compound, it is any compound or mixture of compounds able to diminish the oxygen solubility in a medium containing water and the antioxidant to be stabilized.

The metallic ions sequestering compound is any compound or mixture of compounds that shows a low complexing constant and is effective for capturing and retaining such ions at pH values under 5.0. The sequestering effectiveness comprises its capacity of complexing the metallic ions present in a medium containing water with the antioxidant to be stabilized, whereby minimizing and, preferably, preventing the decomposition catalysis of any antioxidant present in that medium.

The above embodiment of the invention is particularly adequate to obtain the desired stabilization effects and, at the same time, comfort for the user. In addition, it provides stabilization of compositions containing antioxidant compounds such as levogyrous ascorbic acid (LAA), proantocyanidins (OPC), or both, the obtained stabilization being effective for long periods of time.

According to that embodiment of the invention, wherein LAA is present as

antioxidant in a water containing medium, the deoxygenating compound is selected from the glycol group, most preferably among propylene glycol and butilene glycol and mixtures thereof, most preferably propylene glycol.

The metallic ions sequestering compound, in its turn, is selected from the group of ethylenephosphonic acids, its salts and mixtures thereof, or from the group that comprises phosphonates, which include di-, tri-, tetra- and pentavalent acids, their salts and mixtures thereof. More specifically, the compound able to sequester metallic ions can be selected from the group that comprises sodium salt of 1-hydroxyethyliden (1,1 diphosphonic) acid, ethylenediaminetetra (methylenephosphonic) acid, sodium salt of ethylenediaminetetra (methylenphosphonic) acid, sodium salt of diethyleneaminepenta (methylenephosphonic) acid, hydroxyethylidene (1,1 diphosphonic) acid and mixtures thereof. Preferably the metallic ions sequestering agent is 1- hydroxyethylidene (1,1 diphosphonic) acid commercialized under the name Dequest 2010 and supplied by MONSANTO.

In addition to the antioxidant, a preferred composition according to the invention comprises, in the first phase, about 15 to 19% of propylene glycol, about 0.01 to 1% of methyl paraben, about 0.05 to 1% of propyl paraben, from 0.05 to 0.5% of glutathion, from 0.1 to 0.5% of 1- hydroxyethylidene (1,1 diphosphonic) acid, the balance being water in enough quantity to complete 100% of the weight of such phase; wherein the second phase also includes compounds selected from xantham gum thickeners, carbomer and its mixtures, present at about 0.3 to 0.7%, selected methyl paraben, prophil paraben preservatives and mixtures thereof, present at 0.09 to 0.27%.

According to another preferred embodiment of the invention, the first phase of the composition comprises antioxidant compounds in an aqueous solution, which also contains the deoxygenating compound and the metallic ions sequestering agent in a proportion varying from 2500:1 to 50:1. In addition, such first phase further includes LAA reducing agent in a ratio varying from 2520:1 to 20:1 in relation to the sum of the deoxygenating compound and the sequestering agent mass, and in proportion varying from 1:0.02 to 3000:1, in relation to the oxidant compound mass. An advantage resulting from the invention is the LAA outstanding stability as time goes by. When compared to conventional compositions containing the same kind of reducing agent already known by those skilled in the art, the invention permits the use of reducing

compounds in significantly lower quantities, making their use possible in cosmetic and/or pharmaceutical compositions, thus overcoming the prior art disadvantages related to the bad smell aspect and the legal limitations of reducing compound concentration.

Suitable reducing agents are the ones already known for this purpose and include sulphurated compounds, preferably chosen from the group composed of sodium dithionite, sodium disulphides, calcium disulphides, potassium disulphides, and even most preferably, Glutathion, as well as mixtures thereof.

In a commercially adequate cosmetic composition containing, for example, LAA as the antioxidant agent, it is usually employed within a range from about 0.01%, to about 30%, preferably from about 0.5% to about 20%, by weight, while the deoxygenating compound is used within a range from about 10% to about 25%, preferably from about 15% to about 18%, and the sequestering agent is used within a range from about 0.01% to about 0.20%, preferably from about 0.10% to about 0.20%, all the percentages in weight, based on the total weight of the composition. The reducing agent is present in a concentration from about 0.01% to about 0.5%, preferably from about 0.05% to about 0.2%. The amounts of these components will depend, however, on the final objectives of the resulting composition, and they are not restrictive of the invention.

In another embodiment of the invention, a first phase of the composition comprises the LAA as described in the two last embodiments and CPC's present in a range of about 0.001 to 2.2% or even present from about 0.05 to 1.7%, and preferably around 0.3%.

Any of these embodiments for the first phase can be successfully combined together with any one of the second phases described above in proportions from 0.1 to 14:1, preferably between 12:1 to 2:1, and most preferably around 11:1.

The illustrative examples and tests presented below will better describe the present invention. Nevertheless, the illustrated data and procedures relate merely to some embodiment of the present invention and should not be considered as restrictive of its scope.

Example I:

A composition has been prepared comprising a first phase and a second phase, which

comprise:

First Phase

Ingredient	% mass
Water	About 75
Propylene glycol	18
Methyl paraben	0.2
Propyl paraben	0.1
Glutathion	0.1
1- hydroxyethylidene (1,1 diphosphonic) acid (Dequest®)	0.15
LAA	from 1 to 30
OPC	0.3
Modified Xantham Gum	1.4

Second Phase

Ingredient	% mass	
Water	76.20	Vehicle
Xantham Gum	0.27	Thickener
Methyl paraben (Nipagin)	0.18	Preservative
Propyl paraben (Nipazol)	0.09	Preservative
Carbomer (Carbopol 141)	0.27	Thickener
Glycerin	9.09	Moistener
Essence	0.54	Fragrance
Lamellar ceramide	2.12	Skin barrier restructuration agent
Sodium Lauril lactilate	9.09	Disperser
Sodium carboxymethyl betaglycan (Betaglycane)	2.13	Stimulating active

The above composition permits the simultaneous application of selected proportions of compounds as defined in the first phase and in the second phase, what brings a surprising synergy, providing a wide range of benefits to the user. Among the beneficial effects of this product, many of which are explained in the further detailed tests, the following properties of the composition on the skin are detected :

- Improves its exuberance;
- assuages the aging marks of skin (wrinkles and flaccidity);
- improves the skin tint, assuaging the spots appearance;
- stimulates and protect the skin immunological system;
- improves and recover the skin lipidic barrier;
- reduces dark circles;
- improves the aspect of varicose legs;
- improves oral affections (aphthae).

The results of the tests showed below prove the perception of several benefits by users, as well as prove the clinical effectiveness of the product.

A panel has been composed, in a blind study, with 45 volunteers evaluated at 4 moments: immediately after the first application; after one week of use; after one fortnight of use, and after 30 days of use of the product. The supplied product had selected proportions of the first phase to the second phase about 11:1 and had the composition described in Example I above. In all the analyzed moments, the product was evaluated by the consumer and by the doctor. The results of this evaluation are described in Tables I and II, respectively, where the expressed percentages represent the amount of users who noticed that the correspondent benefit has indeed occurred.

Table I: Evaluation of the product performance by the consumer

Attributes	After 1st Application (%)	After 7 days (%)	After 15 days (%)	After 30 days (%)
Protection	8.9	86.7	86.7	93.3
Skin lightening	40.0	80.0	91.1	95.5
More exuberance	86.7	95.5	97.8	97.8
Improvement of softness	93.3	95.5	97.8	97.8
Improvement of tensing action	93.3	95.5	95.5	95.5
Moisture improvement	93.3	97.8	97.8	97.8
Improvement of fine lines (fine wrinkles)	15.5	55.5	64.5	68.9
Cared/Nourished	68.9	97.8	97.8	97.8

Table 2: Evaluation of the product performance by the doctor

Attributes	After 1st Application (%)	After 7 days (%)	After 15 days (%)	After 30 days (%)
Skin lightening	13.3	60.0	68.9	68.9
Improvement of softness	95.5	95.5	97.8	97.8
Improvement of tensing action	82.2	93.3	93.3	93.3
Moisture improvement	95.5	97.8	97.8	97.8
Improvement of fine lines	17.8	55.5	62.2	68.9

It was observed that the above mentioned results are achieved firstly due to the selection of the nature of the antioxidant compounds and of the moisturizing agents

associated to immunomodulators, which, when in contact with skin, produce an advantageous synergetic effect. It is worth observing that in the group of users, all of them indistinctly noticed an improvement greater than 93% for seven out of eight benefits evaluated.

In addition, equally important, the proportion of availability of the first and second phases permitted to find a solution of commitment between the effective antioxidant action and the comfort to the user.

CLAIMS

1. Composition for cosmetic or pharmaceutical use characterized in that it comprises a first phase comprising an antioxidant compound in an aqueous medium and a second phase which comprises a moisturizer compound and an immunomodulator and in that the proportion of said first phase to the second phase is from 6:1 to 14:1.

2. Composition according to claim 1, characterized in that the first phase comprises ascorbic acid as the antioxidant compound present at 1 to 30% by weight, preferably 1 and 10% by weight and the second phase comprises 0.5 to 3.0% of ceramides as moisturizer, and 0.5 to 3.0% of an betaglycane immunomodulator, the proportion between said first and second phases being in the range of 6:1 to 14:1.

3. Composition according to claim 1, characterized in that the first phase comprises ascorbic acid present at 0.0001 to 0.001% by weight.

4. Composition according to claim 1, characterized in that the first phase comprises a mixture of antioxidants comprising ascorbic acid, present at 1 to 20%, and OPC's, present at 0.001 to 2.2%, wherein the second phase comprises 0.5 to 3.0% by weight of ceramides as moisturizer, preferably lamellar ceramides, and 0.5 to 3.0% of betaglycane immunomodulator, the proportion of use between said first and second phases being from 6:1 to 14:1, preferably between 12:1 to 8:1.

5. Composition according to claim 4, characterized in that the antioxidant compound of the first phase comprises 1 to 20% of ascorbic acid preferably between 5 and 18% and 0.001 to 2.2% of OPC's, preferably between 0.01 to 1.7%, wherein the second phase comprises 0.5 to 3.0% of lamellar ceramides as moisturizer, preferably between 1.5 and 2.5%, and the immunomodulator is betaglycane present at a range of 0.5 to 3.0%, preferably 1.5 to 2.5%, the proportion between said first and second phases being from 6:1 to 14:1, preferably between 12:1 to 8:1, and most preferably around 11:1.

6. Composition according to any of the previous claims, characterized in that the ascorbic acid is under the levogyrous molecular form, the OPC's are grape seed oligomers present at about 0.1 to 0.4%, preferably around 0.3% wherein said first and second phas s are maintained separated prior to the moment of use.

7. Composition according to claim 6, characterized in that the first phase also includes about 15 to 19% of propylene glycol, about 0.01 to 1% of methyl paraben, about 0.05 to 1% of propyl paraben, from 0.05 to 0.5% of glutathion, from 0.1 to 0.5% of 1- hydroxyethylidene (1,1 diphosphonic) acid, the balance being water in enough quantity to complete 100% of the weight of such phase; wherein the second phase also includes compounds selected from xantham gum thickeners, carbomer and its mixtures, present at about 0.3 to 0.7%, selected methyl paraben, prophil paraben preservatives and mixtures thereof, present at 0.09 to 0.27%.

8. Composition for cosmetic or pharmaceutical use characterized in that it comprises a first phase comprising an antioxidant compound in an aqueous medium, a deoxygenating compound, a metallic ions sequestering compound, and a reducing agent, and a second phase which comprises a moisturizer compound and an immunomodulator, wherein the application proportion between the first and the second phases ranges from 6:1 to 14:1.

9. Composition according to claim 8, characterized in that the antioxidant compound is selected from the group comprising levogyrous ascorbic acid (LAA) and proanthocyanidins (OPC's).

10. Composition according to any of claims 8 and 9, characterized in that the antioxidant is the LAA.

11. Composition according to any one of claims 8 to 10, characterized in that the antioxidant further comprises proanthocyanidins (OPC's).

12. Composition according to any one of claims 8 to 11, characterized in that the deoxygenating compound is a glycol.

13. Composition according to claim 12, characterized in that the deoxigenatyng compound is chosen from propylene glycol, butilene glycol, and mixtures thereof, most preferably the propylene glycol.

14. Composition according to any one of claims 8 to 13, characterized in that the metallic ions sequestering compound is selected from the group comprising ethylenephosphonic acids, their salts and mixtures thereof, or from the group that comprises phosphonates which include di-, tri, tetra- and pentavalent acids, their salts and mixtures thereof.

15. Composition according to claim 14, characterized in that the metallic ions

sequestering compound is selected from the group which comprises sodium salt of 1-hydroxyethylidene (1,1 diphosphonic) acid, ethylenediaminetetra (methylenephosphonic) acid, sodium salt of ethylenediaminetetra (methylenphosphonic) acid, diethyleneaminepenta (methylenphosphonic) acid, sodium salt of diethyleneaminepenta (methylenephosphonic) acid, hydroxyethylidene (1,1 diphosphonic) acid and mixtures thereof.

16. Composition according to claim 15, characterized in that the metallic ions sequestering compound is 1-hydroxyethyliden (1,1 diphosphonic) acid.

17. Composition according to claim any one of claims 8 to 16, characterized in that the reducing agent is selected from the group comprising sodium dithionite, sodium disulphides, calcium disulphides, potassium disulphides and Glutathion, as well as mixtures thereof.

18. Composition according to claim 17, characterized in that the reducing agent is Glutathion or sodium dithionite.

19. Composition according to claim any one of claims 8 to 18, characterized in that the composition comprises the deoxigenating compound within a range from about 10% to about 25%, the metallic ions sequestering within a range from about 0.01% to about 0.20%, reducing agent in a concentration from about 0.01% to about 0.5%, the antioxidant compound content being from about 0.01% to about 30%, all the percentages being expressed by weight, based on the total weight of the composition.

20. Composition according to claim 19, characterized in that it comprises the deoxygenating compound within a range from about 16% to about 19%, the metallic ions sequestering compound within a range from about 0.10% to about 0.20% and reducing agent at a concentration from about 0.05% to about 0.2%, the antioxidant compound content being from about 0.5% to about 20% by weight.

21. Composition according to claim any one of claims 8 to 20, characterized in that the second phase comprises from 0.5 to 0.3%, most preferably, from 1.5 to 2.5% of moisturizing agents, preferably ceramides, more preferably, lamellar ceramides,: 0.5 to 3.0% and, most preferably, from 1.5 to 2.5% of immunomodulators, preferably betaglycanes, the proportion b tween the first and the second phases being 6:1 to 14:1, preferably from 8:1 to 12:1, and most preferably, about 11:1.

4

TENT COOPERATION TR[illegible]TY

REC'D 23 OCT 2001
WIPO PCT

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
PE-3933		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/BR00/00077	14/07/2000	16/07/1999
International Patent Classification (IPC) or national classification and IPC A61K7/00		
Applicant INDUSTRIA E COMERCIO DE COSMETICOS NATURA LTDA.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 5 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 15 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☒ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15/02/2001	19.10.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Pregetter, M Telephone No. +49 89 2399 8719

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/BR00/00077

I. Basis f th report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-12	as received on	14/09/2001	with letter of	13/09/2001

Claims, No.:

1-21	as received on	14/09/2001	with letter of	13/09/2001

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	2,4,5,7,14-16
	No:	Claims	1,3,6,8-13,17-21
Inventive step (IS)	Yes:	Claims	2,4,5,7,14-16
	No:	Claims	1,3,6,8-13,17-21
Industrial applicability (IA)	Yes:	Claims	1-21
	No:	Claims	

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

Re It m V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: US-A-5 804 168 (MURAD HOWARD) 8 September 1998 (1998-09-08)
   D2: WO 99 33439 A (ROBERTS RICHARD L ;GREENE JAMES A (US); SHAKLEE CORP (US); SIDDIQU) 8 July 1999 (1999-07-08)
   D3: US-A-5 902 591 (HERSTEIN MORRIS) 11 May 1999 (1999-05-11)
   D4: US-A-5 626 883 (PAUL STEPHEN M) 6 May 1997 (1997-05-06)
   D5: US-A-5 094 783 (BROUILLETTE WAYNE J ET AL) 10 March 1992 (1992-03-10)

2. The subject-matter of present claim 1 is not novel according to Article 33(2) PCT. Document D1 discloses aqueous emulsions comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (propylene glycol and/or butylene glycol), a metallic ions sequestering compound (EDTA), and, in the dispersed phase, immunomodulators (retinyl and/or ascorbyl palmitates) and moisturizers/emollients (col.13, l.25-64 and col.15, l.55-col.16, l.24).
   D2 describes an oil-in-water formulation comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (the most common humectants are glycols), a metallic ions sequestering agent, and, in the dispersed phase, immunomodulator (beta glucan) and moisturizers/emollients. Proanthocyanidins in the form of grape seed extract are also present (e.g. example 6).

3. The subject-matter of present claim 8 is not novel according to Article 33(2) PCT. D2 describes an oil-in-water formulation comprising an antioxidant compound in the aqueous phase (magnesium ascorbyl phosphate), a deoxygenating compound (the most common humectants are glycols), a metallic ions sequestering agent, a reducing agent (superoxide dismutase), and, in the dispersed phase, immunomodulator (beta glucan) and moisturizers/emollients (e.g. example 6).

4. None of the documents cited in the search report discloses the combination of ceramides as moisturizer and betaglycan as immunomodulator in a composition comprising an antioxidant.
Since ceramides are not even mentioned in any of the documents cited in the search report, such a combination is furthermore not suggested.
Consequently the subject-matter of claims 2,4 and 5 is considered to be novel and inventive according to Articles 33(2) and (3) PCT.

5. None of the documents cited in the search report suggest to use phosphorous based sequestering agents.
Consequently the subject-matter of claims 7 and 14-16 is considered to be novel and inventive according to Articles 33(2) and (3) PCT.

6. The dependent claims 3, 6, 9-13, 17-21 do not contain any features which, in combination with the features of any claim to which they refer, might establish novelty and an inventive step over D1-D5 (Articles 33(2) and 33(3) PCT).

Re Item VIII

Certain observations on the international application

1. The subject-matter of present claims 1 and 8 is defined by using the term "comprise". This term "comprise" does not exclude the presence of further compounds.

2. The term "phase" can be interpreted in at least two different ways. Firstly, it can be construed in the sense of "liquid phase", "solid phase" or "gaseous phase", secondly it can be seen to mean "hydrophilic phase" versus "hydrophobic phase" and thirdly it can be interpreted to mean several "physically separated entities". For the purpose of examination, all possibilities have to be taken into consideration.

PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 18 April 2001 (18.04.01)	
International application No. PCT/BR00/00077	**Applicant's or agent's file reference** PE-3933
International filing date (day/month/year) 14 July 2000 (14.07.00)	**Priority date** (day/month/year) 16 July 1999 (16.07.99)
Applicant ALCANTARA MARTINS ZUCCHETTI, Roberto et al	

1. The designated Office is hereby notified of its election made:

   [X] in the demand filed with the International Preliminary Examining Authority on:

   15 February 2001 (15.02.01)

   [ ] in a notice effecting later election filed with the International Bureau on:

   _____

2. The election [X] was

   [ ] was not

   made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer Olivia TEFY
Facsimile No.: (41-22) 740.14.35	Telephone No.: (41-22) 338.83.38

INTERNATIONAL SEARCH REPORT

Intern Application No
PCT/BR 00/00077

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K7/00 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 804 168 A (MURAD HOWARD) 8 September 1998 (1998-09-08) column 3, line 30-64 column 4, line 10-12 column 5, line 39-45 column 13, line 26-63 column 15, line 55 -column 16, line 23 claim 1 --- -/--	1,3,8, 12,13

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
8 December 2000	18/12/2000

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bazzanini, R

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

Intern application No
PCT/BR 00/00077

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 33439 A (ROBERTS RICHARD L ;GREENE JAMES A (US); SHAKLEE CORP (US); SIDDIQU) 8 July 1999 (1999-07-08) page 6, line 3-26 page 8, line 10-17 page 10, line 9-14 page 14, line 30 -page 15, line 10 examples 5,6,11,12 page 31, line 13-25 page 32, line 12-18 claims 1-5	1,3,8, 11-13
X	US 5 902 591 A (HERSTEIN MORRIS) 11 May 1999 (1999-05-11) column 2, line 66 -column 3, line 6 column 3, line 15-23 column 4, line 40-46 column 6, line 54-67 column 7, line 48-50 column 11, line 65 -column 13, line 11	1,3,8,12
A	US 5 626 883 A (PAUL STEPHEN M) 6 May 1997 (1997-05-06) column 2, line 50 -column 3, line 10 column 5, line 55-58 column 7, line 61-67 column 8, line 20-23	1-21
A	US 5 094 783 A (BROUILLETTE WAYNE J ET AL) 10 March 1992 (1992-03-10) column 1, line 56-60 column 2, line 60-63	1-21

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims 1,3,6,8-21 have been searched incompletely.

Present claims 1,3,6,8-21 relate to an extremely large number of possible compounds due to the use of very generic words such as "biphasic", "antioxidant", "moisturizer", "immunomodulator" (claim 1) and "deoxygenating compound" (claim 8). Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is to be found, however, for only a very small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds specifically mentioned in the description and in the claims.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

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